III. Remarks

Claims 1-58 were pending in this application with claims 11 and 13-58 being previously withdrawn from consideration. Claims 1-10 and 12 were under active consideration in this application. Claims 3-5 are canceled herein without prejudice to pursuing these claims in a continuing application. Claims 1 and 12 are amended. Upon entry of these amendments, claims 1-2, 6-10 and 12 will be pending and under active consideration.

Claim 1 is amended to restrict the scope of the claim to the elected invention. As amended, claim 1 is drawn to a composition consisting essentially of an effective amount of a β hCG fusion protein comprising the amino acid sequence of SEQ ID NO:2 or a fragment or analog thereof. Claim 12 is amended to be limited to a composition consisting essentially of an effective amount of a β hCG fusion protein consisting of the amino acid sequence of SEQ ID NO:2 or a fragment or analog thereof. Support for the above amendments may be found throughout the specification and the claims as originally filed, notably at page 2, lines 4-9, page 11, lines 26-29 and page 12, line 28 to page 15, line 3.

A. Objections

1. Objection to claim 1 for being drawn to a non-elected invention

At page 3 of Paper No. 10, claim 1 is objected to for being drawn to a non-elected invention. Applicants amend claim 1 herein to be drawn to a composition consisting essentially of an effective amount of a β human chorionic gonadotropin fusion protein comprising the amino acid sequence of SEQ ID NO:2 or a fragment or analog thereof and a chitosan-based adjuvant. In view of claim 1 being amended to be drawn to the elected invention, Applicants respectfully submit that the objection to claim 1 for being drawn to a non-elected invention has been traversed.

2. Objection to specification for failure to provide antecedent basis for the claimed subject matter

At page 3 of Paper No. 10, the specification is objected to as failing to provide antecedent basis for the claimed subject matter. The Examiner asserted that the specification, as filed, does not provide support for the following: (1) the recitation of "βhCG ranges from about 10 μg to

about 500 μg" in original claim 1, (2) the recitation of "βhCG is about 25 μg" in original claim 2, (3) the recitation of "βhCG is about 250 μg" in original claim 3, and (4) the recitation of "consisting essentially of" in original claim 12. Applicants amend claim 1 herein to, among other things, delete the recitation of "βhCG ranges from about 10 μg to about 500 μg." Applicants amend claim 12 herein to, among other things, delete the recitation of "consisting essentially of." Furthermore, Applicants cancel claims 2-3 herein. In view of the foregoing amendments to claims 1 and 12 and the cancellation of claims 2-3, Applicants respectfully request the withdrawal of the objection to the specification for failing to provide antecedent basis for the claimed subject matter.

B. Rejections

1. 35 U.S.C. § 112, first paragraph

a. Rejection of claims 1-10 and 12 for failure to enable one of ordinary skill in the art to practice the claimed invention

At page 3 of Paper No. 10, claims 1-10 and 12 are rejected under 35 U.S.C. § 112, first paragraph for failure to enable one of ordinary skill in the art to practice the claimed invention. At pages 5-6 of Paper No. 10, the Examiner cites various references to allege that the specification does not enable "*any* composition comprising *any* βhCG, *any* fusions, *any* fragments, and *any* analogs thereof." As amended herein, the scope of claim 1 is limited to compositions consisting essentially of an effective amount of a fusion protein comprising the amino acid sequence of SEQ ID NO:2 or a fragment or analog thereof. In view of the narrowing of the scope of claim 1 to compositions consisting essentially of an effective amount of a fusion protein comprising the amino acid sequence of SEQ ID NO:2 or a fragment or analog thereof, Applicant respectfully submits that the rejection of claims 1-10 and 12 under 35 U.S.C. § 112, first paragraph for failure to enable one of ordinary skill in the art to practice the claimed invention has been overcome.

b. Rejection of claims 1-10 and 12 as containing subject matter which was not adequately described in the specification

At page 7 of Paper No. 10, claims 1-10 and 12 are rejected under 35 U.S.C. § 112, first paragraph as containing subject matter which was not described in the specification in such a

way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention. At pages 7-8 of Paper No. 10, the Examiner alleges that with the exception of the fusion polypeptide of SEQ ID NOS:2 and 4, there is insufficient written description for *any* composition comprising "*any* βhCG, *any* fusions, *any* fragments, and *any* analogs thereof." As discussed above, the scope of amended claim 1 is limited to compositions consisting essentially of an effective amount of a fusion protein comprising the amino acid sequence of SEQ ID NO:2 or a fragment or analog thereof. In view of the narrowing of the scope of claim 1 to compositions consisting essentially of an effective amount of a fusion protein comprising the amino acid sequence of SEQ ID NO:2 or a fragment or analog thereof, Applicant respectfully submits that the rejection of claims 1-10 and 12 under 35 U.S.C. § 112, first paragraph has been overcome for containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention.

2. 35 U.S.C. § 103(a)

a. Rejection of claims 1-4 and 6-8 as being unpatentable over WO 91/16922 in view of EP 0368253 and Jones *et al.*

At page 10 of Paper No. 10, claims 1-4 and 6-8 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over WO 91/16922 in view of EP 0368253 and Jones *et al.* At page 10 of Paper No. 10, the Examiner characterizes WO 91/16922 as teaching a composition comprising various analogs of β hCG fusion proteins. At page 10 of Paper No. 10, the Examiner characterizes EP 0368253 as teaching chitosan-based adjuvants for delivering a pharmaceutical such as β hCG. At page 11 of Paper No. 10, the Examiner characterizes Jones *et al.* as teaching a contraceptive vaccine composition comprising a β hCG fragment. At page 11 of Paper No. 10, the Examiner alleges that based on a combination of the cited references it would have been obvious to one of ordinary skill in the art to arrive at a composition comprising a β hCG fusion protein or analog thereof and a chitosan-based adjuvant. Applicant respectfully traverses the rejection. Applicant respectfully submits that the combination of cited references fail to provide a reasonable expectation of success.

To establish a prima facie case of obviousness, the combination of reference teachings must provide a reasonable expectation of success. *See* MPEP 2142; *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). Claims 1-4 and 6-8, as amended, are drawn to a composition (i) consisting essentially of (ii) an effective amount of (iii) a β hCG fusion protein comprising the amino acid sequence of SEQ ID NO:2 or a fragment or analog thereof and (iv) a chitosan-based adjuvant. The transitional phrase "consisting essentially of" limits the scope of the claims to the specified materials and those that do not materially affect the basic and novel characteristics of the claimed invention. *See* MPEP 2111.03; *In re Herz*, 537 F.2d 549, 551-52, 190 USPQ 461, 463 (CCPA 1976). In order to contend that additional materials in the prior art are excluded by the recitation of "consisting essentially of," the applicant has the burden of showing that the introduction of additional components would materially change the characteristics of the invention. *See* MPEP 2111.03.

As discussed in the specification as originally filed at page 2, lines 4-9:

> Because the α subunit of hCG is shared by other hormones, it follows that antisera raised to the entire hCG molecule can cross-react with other hormones, while antisera raised to only the β subunit of hCG exhibit much less cross-reactivity. These results have suggested that the β subunit of hCG would be useful as a highly specific immunological agent for the regulation of mammalian reproduction.

The above-recitation of the specification indicates that the introduction of the α subunit of hCG would materially change the characteristics of the claimed compositions, because the addition of α hCG would lead to unacceptable cross-reactivity with other hormones. The recitation of "consisting essentially of" in amended claim 1 is proper, therefore, to exclude material such as the α subunit of hCG from the claimed compositions.

WO 91/16922 discloses compositions comprising β hCG fusion proteins; however, compositions comprising the β subunit of hCG in the absence of the α subunit of hCG are not contemplated. As discussed at lines 4-8 of page 3 of WO 91/16922,

> The observation that some antibodies bind to epitopes on the hCG beta-subunit only when it is associated with the alpha-subunit suggests that the conformation of the beta-subunit is altered when it combines with the alpha-subunit.

As further discussed at lines 8-13 of page 20 of WO 91/16922,

> It is anticipated that the analogs of the invention which retain regions of tertiary structure present in hCG-beta will be considerably more potent than synthetic peptides in eliciting an immune response to specific domains of hCG and be more efficacious as an immunocontraceptive vaccine.

Taken together, the above recitations from WO 91/16922 strongly suggest that α hCG must be present along with β hCG in order for the production of effective antibodies to β hCG.

Jones *et al.* discloses clinical trials where a vaccine composition comprising a human β hCG fragment conjugated to diphtheria toxin was administered to human females. The clinical trials disclosed in Jones *et al.* are limited to measuring the antibody response in the test subjects. *See* page 1297-1298. There is no indication or suggestion in Jones *et al.* that the vaccine compositions are in fact effective.

A combination of the above teachings from WO 91/16922 and Jones *et al.* would suggest that a vaccine compositions consisting essentially of β hCG would not be effective. As discussed above, WO 91/16922 teaches that the α subunit of hCG must be present for effective production of antibodies to β hCG. As the disclosure of EP 0368253 is limited to chitosan-based adjuvants, there is no indication in the cited references that a vaccine compositions consisting essentially of β hCG would be effective. In view of the cited references failing to provide a reasonable expectation of success, Applicant respectfully submits that the rejection of claims 1-4 and 6-8 under 35 U.S.C. § 103(a) has been overcome based on the amendments herein.

b. Rejection of claims 9-10 as being unpatentable over WO 91/16922 in view of EP 0368253 and Jones *et al.* and further in view of U.S. Patent No. 5,912,000

At page 12 of Paper No. 10, claims 9-10 are rejected under 35 U.S.C. § 103(a) as allegedly being obvious over WO 91/16922 in view of EP 0368253 and Jones *et al.* and further in view of U.S. Patent No. 5,912,000 (the '000 Patent). Applicant respectfully traverses the rejection. The teachings of WO 91/16922, EP 0368253 and Jones *et al.* are discussed above. At page 12 of Paper No. 10, the Examiner characterizes the '000 Patent as teaching various chitosan metal salts recited in claims 9-10. At page 12 of Paper No. 10, the Examiner alleges that based on a combination of the cited references it would have been obvious to one of ordinary skill in the art to arrive at a composition comprising a β hCG fusion protein or analog thereof and the

claimed chitosan-based adjuvants. Applicant respectfully traverses the rejection. Applicant respectfully submits that the combination of cited references fail to provide a reasonable expectation of success.

As discussed above, the disclosure of Jones *et al.* is limited to measuring antibody response in test subjects administered a vaccine composition comprising a human β hCG fragment conjugated to diphtheria toxin. As also discussed above, the teachings of WO 91/16922 indicate that the α subunit of hCG must be present for the effective production of antibodies to β hCG. The disclosure of EP 0368253 and the '000 Patent is limited to chitosan-based adjuvants. In view of the cited references failing to provide a reasonable expectation that a vaccine composition consisting essentially of β hCG would be effective, Applicant respectfully submits that the rejection of claims 9-10 under 35 U.S.C. § 103(a) has been overcome based on the amendments herein.

c. Rejection of claim 12 as being unpatentable over WO 91/16922 in view of EP 0368253 and Jones *et al.* and further in view of U.S. Patent No. 5,602,005

At page 13 of Paper No. 10, claim 12 is rejected under 35 U.S.C. § 103(a) as allegedly being obvious over WO 91/16922 in view of EP 0368253 and Jones *et al.* and further in view of U.S. Patent No. 5,602,005 (the '005 Patent). Applicant respectfully traverses the rejection. The teachings of WO 91/16922, EP 0368253 and Jones *et al.* are discussed above. At page 13 of Paper No. 10, the Examiner characterizes the '005 Patent as teaching a recombinant fusion protein consisting of human acrosomal sperm antigen 10 (SP-10) joined to a β-galactosidase protein. At page 13 of Paper No. 10, the Examiner alleges that based on a combination of the cited references it would have been obvious to one of ordinary skill in the art to arrive at a composition consisting essentially of a β hCG fusion protein or analog thereof and the claimed chitosan-based adjuvants. Applicant respectfully traverses the rejection. Applicant respectfully submits that the combination of cited references fail to provide a reasonable expectation of success.

As discussed above, the disclosure of Jones *et al.* is limited to measuring antibody response in test subjects administered a vaccine composition comprising a human β hCG fragment conjugated to diphtheria toxin. As also discussed above, the teachings of WO 91/16922 indicate that the α subunit of hCG must be present for the effective production of

antibodies to β hCG. The disclosure of EP 0368253 is limited to chitosan-based adjuvants. The disclosure of the '005 Patent is limited to fusion proteins consisting of SP-10. In view of the cited references failing to provide a reasonable expectation that a vaccine composition consisting essentially of β hCG would be effective, Applicant respectfully submits that the rejection of claim 12 under 35 U.S.C. § 103(a) has been overcome based on the amendments herein.

C. Conclusion

In view of the above remarks, Applicant respectfully submits that the present application is in good and proper order for allowance and early notification to this effect is solicited. If, in the opinion of the Examiner, a telephone conference would expedite prosecution of the instant application, the Examiner is encouraged to call the undersigned at the number listed below.

Respectfully submitted,

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APPENDIX A

For the convenience of the Examiner, Applicant presents herewith a copy of the claims that will be pending and under active consideration upon entry of the present amendments.

1. (currently amended) A composition consisting essentially of an effective amount of a β human chorionic gonadotropin fusion protein comprising the amino acid sequence of SEQ ID NO:2 or a fragment or analog thereof and a chitosan-based adjuvant.

2. (original) The composition of claim 1 wherein the amount of βhCG is about 25 μg.

6. (original) The composition of claim 1 wherein the chitosan-based adjuvant comprises an emulsion of chitosan, sodium hydroxide, a biodegradable oil, a surfactant, and an aqueous buffer.

7. (original) The composition of claim 6 wherein the biodegradable oil is squalene.

8. (original) The composition of claim 6 wherein the ratio of βhCG proteins and/or fusions, fragments or analogs thereof to adjuvant is in the range of about 1:20 (w:w) to about 1:1500 (w/w).

9. (original) The composition of claim 1 wherein the adjuvant comprises chitosan, a metal salt, and an aqueous buffer.

10. (original) The composition of claim 9 wherein the metal salt is selected from the group consisting of zinc acetate, nickel sulfate, and copper sulfate.

12. (original) The composition of claim 1 wherein the β human chorionic gonadotropin fusion protein consists of the sequence set forth in SEQ ID NO:2 .